"THE EFFECT OF IRON REPLACEMENT THERAPY ON HYPOTHYROID PATIENTS WITH IRON DEFECIENCY ANEMIA"

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ABSTRACT-

Introduction: One of the major public health problems faced by developing countries in the world is a micronutrient deficiency. Such deficiencies have an adverse impact on the growth and development of vulnerable populations such as infants, children, pregnant and lactating women. Iron is the most abundant trace element, and amongst them iron deficiency can have detrimental effects on various biological processes in the human body.[1]

Iron and thyroid metabolism are closely intricately linked to each other, several studies have demonstrated that iron deficiency is an overlooked cause of hypothyroidism. It may result in significantly lowering the circulating levels of both thyroxine and triiodothyronine, It is also reported to decrease the peripheral conversion of T4 to T3.[2] Estimation of iron profile may be of use in patients of the hypothyroidism, as iron deficiency itself may be the underlying cause of hypothyroidism. It reduces the over correction of thyroid deficiency when the real culprit is the iron deficiency which needs the correction.[3]

Objectives of the study:

1. To study relationship between serum ferritin level and thyroid function in iron deficiency anemia.

2. To evaluate the effect of iron replacement therapy on the Hypothyroidism patients with Iron deficiency Anemia.

Materials and Methods: This was a hospital based longitudinal follow up study in which 51 patients of hypothyroidism with iron deficiency were included. Iron deficiency defined by a serum ferritin level less than 30µg/L. Anemia is defined as a hemoglobin level of 11gm/dL or less in women and 13gm/dL or less in men. Hypothyroidism was considered when TSH level more than 4.4 IU/mL. Patients were given iron supplementation of ferrous sulphate 200mg for 3 months and patients were followed up with repeat levels of thyroid profile, serum ferritin levels and these parameters were compared with the initial levels.

Results: In this study maximum numbers of the patients were in the age group of 20-30 years. Majority of patients were females as compared to males with a female predominance of 90.2%. Among 51 patients 69% patients had subclinical hypothyroidism and 31% patients had clinical hypothyroidism. 65% of patients of hypothyroidism including subclinical and clinical hypothyroidism improved after treatment, 35% patients did not improve. In present study pre and post treatment serum ferritin and TSH had shown negative correlation. There is positive correlation between serum ferritin and TT3, TT4, FT3, FT4 in both pre treatment and post treatment groups.

Conclusion: In our study it was found that there was an association between serum ferritin and thyroid hormones. Treatment of the iron deficiency in the hypothyroid patients led to a significant improvement in the functioning of thyroid hormones evidenced by improvement in thyroid parameters.

INTRODUCTION:

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Estimation of iron profile may be of use in patients of the hypothyroidism, as iron deficiency itself may be the underlying cause of hypothyroidism. It reduces the over correction of thyroid deficiency when the real culprit is the iron deficiency which needs the correction.

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MATERIALS AND METHODS:

This study included patients of hypothyroidism with iron deficiency anemia, 18years or above attended the Department of General Medicine of R. L. Jalappa hospital and research centre Tamaka, Kolar between December 2016 and September 2018.

Hospital based longitudinal follow up study. 51 patients of hypothyroidism with iron deficiency anemia, sample size of 51 was estimated with each factor and with 80% power and 95% confidence level. The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Sample size estimated based on CIMT to detect mean CIMT thickness of 0.10 the sample size required 41 per group with 80% error and 95% confidence level. Page 35 Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Inclusion criteria: 1. Patients aged more than 18 years. 2. Patients diagnosed to have hypothyroidism with iron deficiency anemia.

Exclusion criteria: 1. pregnant women. 2. Patients on treatment for hypothyroidism. 3. Patient with a positive Anti TPO antibody.

Iron deficiency defined by a serum ferritin level less than 30µg/L, mean corpuscular volume (MCV) less than 76fL. Anemia is defined as a hemoglobin level of 11gm/dL or less in women and 13gm/dL or less in men. Hypothyroidism was be considered when TSH level more than 4.4 IU/mL. Reference values of study parameters: TSH= 0.4- 4.4 IU/mL TT3= 84-172ng/dL TT4= 4.5 – 12.5 ng/dL FT3 = 1.8-4.71 pg/mL FT4 = 0.8- 1.9ng/dL Serum ferritin level= 30-300 µg/L. Patient was given iron supplementation of ferrous sulphate 200mg for 3 month and patient was followed up with repeat levels of thyroid profile, serum ferritin levels and this parameters were compared with the initial levels. Serum Ferritin and Serum Thyroid function were estimated by immune turbidometric method and electrochemiluminescent immunoassay (ECLIA) respectively.

RESULTS:

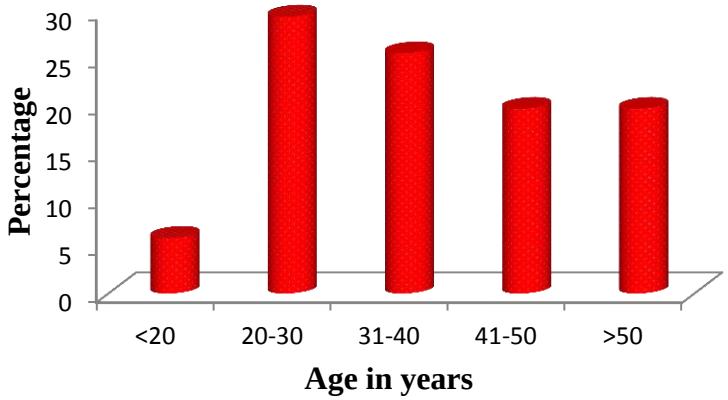

Figure 1: Age distribution of patients studied

Table 1: Gender distribution of patients studied

Gender	No. of patients	%
Female	46	90.2
Male	5	9.8
Total	51	100.0

Table 2: Pre Treatment_Pearson correlation- serum ferritin with Thyroid functions

Pre Treatment	r value	P value
Serum Ferritin **vs** Hemoglobin (g/dl)	0.812	<0.001**
Serum Ferritin **vs** TSH	-0.573	<0.001**
Serum Ferritin **vs** TT3	0.511	<0.001**
Serum Ferritin **vs** TT4	0.448	0.001**
Serum Ferritin **vs** FT3	0.388	0.005**
Serum Ferritin **vs** FT4	0.414	0.003**

Table 3: Post Treatment Serum Ferritin with Thyroid functions

Post Treatment	r value	P value
Serum Ferritin **vs** Hemoglobin (g/dl)	0.853	<0.001**
Serum Ferritin **vs** TSH	-0.073	0.612
Serum Ferritin **vs** TT3	0.351	0.012*
Serum Ferritin **vs** TT4	0.441	0.001**
Serum Ferritin **vs** FT3	0.301	0.032*
Serum Ferritin **vs** FT4	0.421	0.002**

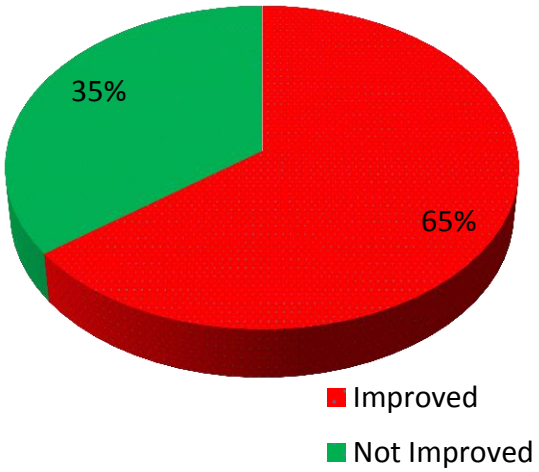

Figure 2: Improved

Table 4: Serum Ferritin- An assessment at pre and post treatment of patients studied

Serum Ferritin (µg/L)	Pre Treatment	Post Treatment	% difference
<10	7(13.7%)	0(0%)	-13.7%
10-20	34(66.7%)	0(0%)	-66.7%
21-30	10(19.6%)	0(0%)	-19.6%
>30	0(0%)	51(100%)	100.0%
Total	51(100%)	51(100%)	-

Table 5: A comparison of clinical parameters at pre and post treatment

variables	Pre Treatment	Post Treatment	difference	t value	P value
Hemoglobin (g/dl)	8.34±0.70	11.77±0.72	3.44	48.67	<0.001**
Serum Ferritin	15.55±5.14	183.20±62.02	167.65	20.19	<0.001**
TSH	9.13±4.78	4.15±1.45	4.98	8.78	<0.001**
TT3	85.66±15.33	88.90±14.24	3.24	5.27	<0.001**
TT4	6.15±2.29	7.29±1.25	1.14	5.89	<0.001**
FT3	2.62±1.09	3.17±0.55	0.55	5.34	<0.001**
FT4	0.97±0.44	1.15±0.27	0.18	5.57	<0.001**

DISCUSSION:

Patients in the age group of 19-70 years were selected. The peak incidence of hypothyroidism with iron deficiency was observed in age group of 21-30 years (29.4%), followed by the age group of 31-40 years (25.5%) with Mean ± SD: 38.55±14.36 years. It was observed that the patients in our study had a lower mean age group as compared to the patients in a study that was done by Mehmet E et al, in which the mean age range was higher, and was found to have a mean age of 44.00±14.36 years.[4]

Several studies by Kostoglou I et al, Surks MI et al and Dillman E et al done in this regard showed that the female patients affected with hypothyroidism were more than the male patients.[5, 6, 7] Our study had similar findings with a female population of 90.2% and a male population of 9.8%.

Serum ferritin and TSH showed a negative correlation in both the pretreatment and the post treatment patients of -0.574 and -0.073 respectively. Similar findings were observed by Padmaja TVK et al which included 91 patients with iron deficiency and hypothyroid showed a negative correlation between serum ferritin and TSH.[8] Akhter S et al also showed a similar correlation between serum ferritin and TSH.[9] However Yavuz O et al showed no correlation between serum TSH and serum ferritin level.[10]

There was a positive correlation between serum ferritin and TT3, TT4, FT3 and FT4. Akhter S et al showed similar results, however it was not statistically significant.[9] The post treatment serum ferritin and TT4, TT3, FT3 and FT4 showed a positive correlation with a statistically significant p-value. Beard JL et al also showed that there was a positive correlation between serum ferritin and FT3, FT4 level after treatment.[11] Another study by Tieboon P et al which included children the pre and post iron replacement therapy did not show any statistically significant value, however this difference can be attributed to difference in demographic region and age.[12]

Out of 51 patient of hypothyroidism with iron deficiency anaemia, 33 (64.7%) patient improved with the iron replacement therapy and 18 (35.3%) patient did not show improvement with iron replacement therapy. Contradictory to this, a study done by Gokdeniz E et al, showed no improvement with iron replacement therapy among the groups that were studied.[13]

In this study serum ferritin level was 15.55±5.14µg/L in the pretrement group and it improved to 183.20±62.02 µg/L in the post treatment group which was statistically significant. Another observational study by Sachadeva A et al showed serum ferritin level of 21.08±3.18 µg/L in hypothyroid patients which was near similar to the current study.[14]

CONCLUSION:

In our study it was found that there was an association between serum ferritin and thyroid hormones. Treatment of the iron deficiency in the hypothyroid patients led to a significant improvement in the functioning of thyroid hormones evidenced by improvement in thyroid parameters such as TSH, TT3, TT4, FT3 and FT4.

Iron deficiency anemia was found to be more in subclinical hypothyroidism patients than the clinical hypothyroidism patients. Moreover the thyroid function improved in the subclinical hypothyroidism patients as compared to clinical hypothyroidism patients.

Thereby, supplementing iron in patients with hypothyroidism with iron deficiency anemia reduces the burden of overuse of thyroid hormone replacement therapy and reduces the complication associated with supplementation thyroxine hormone.

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